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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/735,099	12/11/2000	Johannes Dapprich	22650-001 CIP	5343

30623 7590 06/13/2005

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EXAMINER	
FORMAN, BETTY J	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 06/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/735,099	DAPPRICH ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-12,15-18,21,39,40 and 42-101* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-12,15-18,21,39,40 and 42-101* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5.0-0.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5 April 2005 has been entered.

Status of the Claims

2. This action is in response to papers filed 5 April 2005 in which claims 1, 3, 18, 39, 42, 43, 47 and 50 were amended, claim 19 was canceled and claims 56-101 were added. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action dated 5 November 2004, not reiterated below, are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed but are deemed moot in view of the amendments, withdrawn rejections and new grounds for rejection. New grounds for rejection are discussed.

Claims 1, 3-12, 15-18, 21, 39-40 and 42-101 are under prosecution.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1, 3 –12, 15-18, 21, 39-40, 42-60, 62-64, 68, 71-72, 75-81, 83-85, 89, 92-93 and 96-97 are rejected under 35 U.S.C. 102(b) as being anticipated by Montforte et al (WO 98/26095, published 18 June 1998).

Regarding Claim 1, Montforte et al disclose a method for separating a target molecule, the target comprising genomic or RNA (page 53, lines 12-15) and a target sequence and distinguishing element (e.g. SNP, page 54). The method comprising the steps of contacting a population of nucleic acids with a targeting element (probe) that binds adjacent to the mutation, and selectively and covalently attaching a separation group to the targeting element (biotinylated nucleotide, page 55, lines 6-19), immobilizing the polynucleotide and targeting element via separation group (page 11, lines 28-32 and e.g. biotin-avidin, page 54, lines 24-29) and removing the immobilized complex from the population of nucleic acids i.e. partitioning (pages 54-56).

Regarding Claim 3, Montforte et al disclose the method wherein the target sequence is immediately adjacent the distinguishing element (page 54, lines 5-6).

Regarding Claim 4, Montforte et al disclose the method wherein the targeting element comprises a nucleic acid sequence (i.e. probe, page 54, line 5).

Regarding Claim 5, Montforte et al disclose the method wherein the targeting element comprises an oligonucleotide (i.e. probe, page 54, line 5).

Regarding Claim 6, Montforte et al disclose the method wherein the oligonucleotide has an extendable end (page 54, lines 5-7).

Regarding Claim 7, Montforte et al disclose the method wherein the separation group is an immobilizable nucleotide (page 54, lines 24-29 and page 55, lines 6-7).

Regarding Claim 8, Montforte et al disclose the method wherein the separation group is a biotinylated nucleotide (page 54, lines 24-29 and page 55, lines 6-7).

Regarding Claim 9, Montforte et al disclose the method wherein the first separation group is attached by extending the oligonucleotide with a polymerase in the presence of biotinylated nucleotides (page 54, lines 5-7 and page 55, lines 6-7).

Regarding Claim 10, Montforte et al disclose the method wherein the targeting element is an oligonucleotide (i.e. probe, page 54, line 5).

Regarding Claim 11, Montforte et al disclose the method wherein the separation group is an immobilizable nucleotide (page 54, lines 24-29 and page 55, lines 6-7).

Regarding Claim 12, Montforte et al disclose the method wherein the immobilizable nucleotide is a biotinylated nucleotide (page 54, lines 24-29 and page 55, lines 6-7).

Regarding Claim 15, Montforte et al disclose the method wherein the population of nucleotides is RNA (page 53, lines 13-15).

Regarding Claim 16, Montforte et al disclose the method wherein the distinguishing element is a SNP (page 54, lines 1-4).

Regarding Claim 17, Montforte et al disclose the method wherein said partitioning substrate is a bead, particle or glass surface (page 43, lines 27-32).

Regarding Claim 18, Montforte et al disclose the method further comprising contacting the population with a second targeting element i.e. multiplex detection using a large number of probes (page 55, liens 4-5).

Regarding Claim 21, Montforte et al disclose the method wherein the population is genomic DNA (page 53, lines 12-14).

Regarding Claim 39, Montforte et al disclose a method for separating a target molecule, the target comprising genomic or RNA (page 53, lines 12-15) and a target sequence and distinguishing element (e.g. SNP, page 54). The method comprising the steps of contacting a population of nucleic acids with a targeting element (probe) that binds adjacent to the

mutation, and selectively and covalently attaching a separation group to the targeting element (biotinylated nucleotide, page 55, lines 6-19), immobilizing the polynucleotide and targeting element via separation group (e.g. biotin-avidin, page 54, lines 24-29) and removing the immobilized complex from the population of nucleic acids i.e. partitioning (pages 54-56).

Regarding Claim 40, Montforte et al disclose the method wherein the oligonucleotide targeting element is has an extendable 3' end (page 54, lines 5-10).

Regarding Claim 42, Montforte et al disclose the method wherein the immobilizable nucleotide is a biotinylated nucleotide and the separation groups is attached by oligonucleotide extension using a polymerase (page 54, lines 5-10 and page 55, lines 6-7).

Regarding Claim 43, Montforte et al disclose a method for separating a target molecule, the target comprising genomic or RNA (page 53, lines 12-15) and a target sequence and distinguishing element (e.g. SNP, page 54). The method comprising the steps of contacting a population of nucleic acids with a targeting element (probe) that binds adjacent to the mutation, and selectively and covalently attaching a separation group to the targeting element (biotinylated nucleotide, page 55, lines 6-19), immobilizing the polynucleotide and targeting element via separation group (e.g. biotin-avidin, page 54, lines 24-29) and removing the immobilized complex from the population of nucleic acids i.e. partitioning (pages 54-56).

Regarding Claim 44, Montforte et al disclose the method wherein the sequence of interest is an amplified sequence (page 53, line 14).

Regarding Claim 45, Montforte et al disclose the method wherein the attachment of the separation group occurs through ligation (page 58, lines 31-32).

Regarding Claim 46, Montforte et al disclose the method wherein the attachment of the separation group occurs using a polymerase (page 54, lines 5-7 and page 58, lines 31-32).

Regarding Claim 47, Montforte et al disclose a method for separating a target molecule, the target comprising genomic DNA (page 53, lines 12-15) and a target sequence and distinguishing element (e.g. SNP, page 54). The method comprising the steps of contacting a

population of nucleic acids with a targeting element (probe) that binds adjacent to the mutation, and selectively and covalently attaching a separation group to the targeting element (biotinylated nucleotide, page 55, lines 6-19), immobilizing the polynucleotide and targeting element via separation group (e.g. biotin-avidin, page 54, lines 24-29) and removing the immobilized complex from the population of nucleic acids i.e. partitioning (pages 54-56).

Regarding Claim 48, Montforte et al disclose the method wherein the distinguishing element is a polymorphism (page 54, lines 1-4).

Regarding Claim 49, Montforte et al disclose the method wherein the polymorphism is a SNP (page 54, lines 1-4).

Regarding Claim 50, Montforte et al disclose a method for separating a target molecule, the target comprising genomic DNA or RNA (page 53, lines 12-15) and a target sequence and distinguishing element (e.g. SNP, page 54). The method comprising the steps of contacting a population of nucleic acids with a targeting element comprising a covalently attached separation group (biotinylated nucleotide) that binds adjacent to the mutation, and stabilizing the binding of the targeting element (i.e. the primer extension or ligation increases stability, page 59, lines 3-10), immobilizing the polynucleotide and targeting element via separation group (e.g. biotin-avidin, page 54, lines 24-29) and removing the immobilized complex from the population of nucleic acids i.e. partitioning (pages 54-56).

Regarding Claim 51, Montforte et al disclose the method wherein the targeting element is an oligonucleotide (i.e. probe, page 54, line 5).

Regarding Claim 52, Montforte et al disclose the method wherein the targeting element binds within 20 nucleotides (i.e. adjacent, page 54, line 5).

Regarding Claim 53, Montforte et al disclose the method wherein the distinguishing element is a polymorphism (page 54, lines 1-4).

Regarding Claim 54, Montforte et al disclose the method wherein the polymorphism is a SNP (page 54, lines 1-4).

Regarding Claim 55, Montforte et al disclose the method wherein the targeting element-separation group is a biotinylated nucleotide (page 54, lines 24-29 and page 55, lines 6-7).

Regarding Claim 56, Montforte et al disclose the method wherein the population is genomic DNA, the targeting element is an oligonucleotide and the distinguishing element is a polymorphism (page 54-55).

Regarding Claim 57, Montforte et al disclose the method wherein the target sequence is adjacent the distinguishing element and the separation group comprises a terminating nucleotide complementary to the polymorphism attached via oligonucleotide extension (page 54-55).

Regarding Claim 58, Montforte et al disclose the method wherein the 3' terminus of the oligonucleotide is complementary to the polymorphism (i.e. after extension, page 54, lines 5-7).

Regarding Claim 59, Montforte et al disclose the method wherein the separation group comprises a non-terminating nucleotide and is attached by extending the targeting element in the presence of the separation group (i.e. an oligonucleotide separation group having biotin or digoxigenin is attached to the probe by extension with a ligase, page 6, lines 16-31).

Regarding Claim 60, Montforte et al disclose the method wherein the separation group is a modified non-terminating nucleotide (i.e. modified to contain a biotin or digoxigenin functional group, page 6, lines 23-25).

Regarding Claim 62, Montforte et al disclose the method wherein the separation group comprises a cleavable linker (page 54, lines 11-30).

Regarding Claim 63, Montforte et al disclose the method wherein the targeting element comprises a cleavable linker (page 54, lines 12-18).

Regarding Claim 64, Montforte et al disclose the method wherein the separation group comprises a non-terminating nucleotide and is attached by extending the targeting element in the presence of the separation group (i.e. an oligonucleotide separation group having biotin or digoxigenin is attached to the probe by extension with a ligase, page 6, lines 16-31).

Regarding Claim 68, Montforte et al disclose the method wherein the substrate is a streptavidin coated surface, the targeting element is an oligonucleotide, the non-terminating nucleotide is biotinylated and extending the oligonucleotide links the polynucleotide to the substrate (i.e. an oligonucleotide separation group having biotin or digoxigenin is attached to the probe by extension with a ligase, page 6, lines 16-31).

Regarding Claim 71, Montforte et al disclose the method wherein prior to step (b), the genomic DNA is denatured (i.e. via PCR cycling conditions, Examples 6-8).

Regarding Claim 72, Montforte et al disclose the method wherein prior to step (b), the genomic DNA is denatured with heat (i.e. via PCR cycling conditions, Examples 6-8).

Regarding Claim 75, Montforte et al disclose the method wherein the polynucleotide is characterized (i.e. following release of the mass label the SNP is identified, Example 6-8).

Regarding Claim 76, Montforte et al disclose the method wherein characterization identifies haplotype (i.e. following release of the mass label the SNP is identified, Example 6-8).

Regarding Claim 77, Montforte et al disclose the method wherein the DNA is a plasmid i.e. insert within a clone (page 53, lines 14-15).

Regarding Claim 78, Montforte et al disclose the method wherein the population is genomic DNA, the targeting element is an oligonucleotide and the distinguishing element is a SNP (page 54-55).

Regarding Claim 79, Montforte et al disclose the method wherein the 3' terminus of the oligonucleotide is complementary to the polymorphism (i.e. after extension, page 54, lines 5-7).

Regarding Claim 80, Montforte et al disclose the method wherein the separation group comprises a non-terminating nucleotide and is attached by extending the targeting element in the presence of the separation group (i.e. an oligonucleotide separation group having biotin or digoxigenin is attached to the probe by extension with a ligase, page 6, lines 16-31).

Regarding Claim 81, Montforte et al disclose the method wherein the separation group is a modified non-terminating nucleotide (i.e. modified to contain a biotin or digoxigenin functional group, page 6, lines 23-25).

Regarding Claim 83, Montforte et al disclose the method wherein the separation group comprises a cleavable linker (page 54, lines 11-30).

Regarding Claim 84, Montforte et al disclose the method wherein the targeting element comprises a cleavable linker (page 54, lines 12-18).

Regarding Claim 85, Montforte et al disclose the method wherein the separation group comprises a non-terminating nucleotide and is attached by extending the targeting element in the presence of the separation group (i.e. an oligonucleotide separation group having biotin or digoxigenin is attached to the probe by extension with a ligase, page 6, lines 16-31).

Regarding Claim 89, Montforte et al disclose the method wherein the substrate is a streptavidin coated surface, the targeting element is an oligonucleotide, the non-terminating nucleotide is biotinylated and extending the oligonucleotide links the polynucleotide to the substrate (i.e. an oligonucleotide separation group having biotin or digoxigenin is attached to the probe by extension with a ligase, page 6, lines 16-31).

Regarding Claim 92, Montforte et al disclose the method wherein prior to step (b), the genomic DNA is denatured (i.e. via PCR cycling conditions, Examples 6-8).

Regarding Claim 93, Montforte et al disclose the method wherein prior to step (b), the genomic DNA is denatured with heat (i.e. via PCR cycling conditions, Examples 6-8).

Regarding Claim 96, Montforte et al disclose the method wherein the polynucleotide is characterized (i.e. following release of the mass label the SNP is identified, Example 6-8).

Regarding Claim 97, Montforte et al disclose the method wherein characterization identifies haplotype (i.e. following release of the mass label the SNP is identified, Example 6-8).

5. Claims 50-52 and 55 are rejected under 35 U.S.C. 102(e) as being anticipated by Lundeberg et al (U.S. Patent No. 6,482,592, filed 15 September 1998).

Regarding Claim 50, Lundeberg et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules comprising the polynucleotide having a first target sequence within 100 nucleotides of a distinguishing element (i.e. module-binding site), contacting the population of nucleic acid molecules with a first targeting element containing a separation group (module) which specifically binds to the polynucleotide molecule, selectively stabilizing the binding of the targeting element (via additional modules, Column 4, lines 9-11) and immobilizing the polynucleotide-targeting element-separation group complex and isolating the complex (Column 11, lines 7-14).

Regarding Claim 51, Lundeberg et al disclose the method wherein the targeting element is an oligonucleotide (Column 5, lines 1-17).

Regarding Claim 52, Lundeberg et al disclose the method wherein the targeting element binds within 20 nucleotides of the distinguishing element (i.e. adjacent, Column 11, lines 21-43).

Regarding Claim 55, Lundeberg et al disclose the method wherein the targeting element-separation group comprises a biotinylated nucleotide i.e. biotinylated oligo (Column 12, lines 42-51).

Response to Arguments

6. Applicant asserts that Lundeburg et al do not teach the claims as amended wherein the polynucleotide is genomic DNA or RNA and comprises a distinguishing element that distinguishes from "a nearly identical sequence (e.g. the same gene of paternal origin)." The argument has been considered but is not found persuasive. First, Lundeburg et al specifically teaches genomic DNA or RNA (Column 4, lines 43-45). Second, the claims are not limited to "the same gene of paternal origin" as asserted. Therefore, the argument is not commensurate

in scope with the claims. Furthermore, in contrast to the asserted "same gene", claims merely require an element that distinguished from a "nearly identical" sequence. The claims nor specification define the meets and bounds of the phrase "nearly identical". The word "nearly" is a relative term which defines the sequences as non-identical but does not define the degree of dissimilarity. Because the claims do not define the phrase "nearly identical" the phrase is given its broadest reasonable interpretation. Lundeburg et al specifically teach their method provides detection sensitivity at the single nucleotide level via primer extension (Abstract). This method distinguishes sequences hybridized to primers which are extended from those sequences having non-extended primers. Therefore, Lundeburg et al teaches the nearly identical as broadly claimed.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1, 3-12, 15-18, 21, 39-40, 42-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ju et al U.S. Patent No. 5,876,936, issued 2 March 1999) in view of Engelhardt et al (U.S. Patent No. 6,221,581, filed 7 June 1995).

Regarding Claim 1, Ju et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules (i.e. mixture of

differently sized primer extension products, Column 6, lines 13-47) comprising the polynucleotide having a first target sequence within 100 nucleotides of a distinguishing element (primer binding site adjacent to site of terminator incorporation, Column 5, lines 11-13), contacting the population of nucleic acid molecules with a first targeting element (i.e. primer) which specifically binds to the polynucleotide molecule, selectively attaching a separation group (biotinylated ddNTP) to the targeting element bound to the polynucleotide wherein the attaching only occurs when the primer is bound to the polynucleotide, immobilizing the polynucleotide-targeting element-separation group via the incorporated ddNTP (Column 7, lines 5-32; Column 9, lines 36-53 and Claim 18, steps a-g). Ju et al specifically teach the "entire sequencing reaction mixtures" are combined with streptavidin coated beads and the beads are immobilized. Following immobilization, the DNA fragments are removed (Column 7, lines 5-32 and Column 9, lines 36-53). This subsequent step of removing the DNA fragments is encompassed by the open claim language "comprising".

Ju et al teach the method wherein the population comprises DNA molecules but they are silent regarding RNA or specific DNAs (e.g. cDNA or genomic DNA) or specific distinguishing elements (e.g. SNP). However, Engelhardt et al teach a similar method of separating a polynucleotide (Claims 112-116) wherein the DNA encompasses any DNA and they further teach the method is useful for detecting SNPs which clearly suggests that SNPs are important elements of genomic DNA (Column 2, lines 17-23; Column 3, lines 22-45; and Column 12, lines 26-50). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the SNP separation/detection of Engelhardt to the genomic DNA analysis of Ju et al based on the known importance of SNPs for the obvious benefits of separating and detecting important genomic DNA as suggested by Engelhardt (Column 2, lines 17-23).

Regarding Claim 3, Ju et al disclose the method wherein the targeting element binds to the distinguishing element (i.e. adjacent to site of terminator incorporation, Column 5, lines 11-13),

Regarding Claim 4, Ju et al disclose the method wherein the targeting element comprises a nucleic acid sequence (i.e. primer, Column 5, lines 3-11).

Regarding Claim 5, Ju et al disclose the method wherein the targeting element comprises an oligonucleotide (i.e. primer, Column 5, lines 3-11).

Regarding Claim 6, Ju et al disclose the method wherein the targeting element comprises an extendable 3' hydroxy terminus (i.e. primer, Column 5, lines 3-11).

Regarding Claim 7, Ju et al disclose the method wherein the separation group is an immobilizable nucleotide i.e. biotinylated ddNTP (Column 6, lines 40-47).

Regarding Claim 8, Ju et al disclose the method wherein the separation group is an immobilizable nucleotide i.e. biotinylated ddNTP (Column 6, lines 40-47).

Regarding Claim 9, Ju et al disclose the method wherein the first separation group is attached to the targeting element by extending the oligonucleotide with a polymerase in the presence of biotinylated nucleotide forming an extended oligonucleotide containing immobilizable nucleotide (Column 6, lines 17-47).

Regarding Claim 10, Ju et al disclose the method wherein the targeting element comprises an oligonucleotide (i.e. primer, Column 5, lines 3-11).

Regarding Claim 11, Ju et al disclose the method wherein the separation group is an immobilizable nucleotide i.e. biotinylated ddNTP (Column 6, lines 40-47).

Regarding Claim 12, Ju et al disclose the method wherein the separation group is an immobilizable nucleotide i.e. biotinylated ddNTP (Column 6, lines 40-47).

Regarding Claim 13, Ju et al disclose the method wherein the population of molecules is DNA (Column 6, lines 17-22).

Regarding Claim 17, Ju et al disclose the method wherein the substrate is a particle, bead or magnetic bead (Column 7, lines 19-27).

Regarding Claim 18, Ju et al disclose the method further comprising contacting the population with a second targeting element simultaneously and capturing via a second separation group (Column 7, lines 5-32; Column 9, lines 36-53 and Claim 18, steps a-g).

Regarding Claim 39, Ju et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules (i.e. mixture of differently sized primer extension products, Column 6, lines 13-47) comprising the polynucleotide having a first target sequence within 100 nucleotides of a distinguishing element (primer binding site adjacent to site of terminator incorporation, Column 5, lines 11-13), contacting the population of nucleic acid molecules with a first targeting element (i.e. primer) which specifically binds to the polynucleotide molecule, selectively attaching a separation group comprising an immobilizable nucleotide (biotinylated ddNTP) to the targeting element bound to the polynucleotide wherein the attaching only occurs when the primer is bound to the polynucleotide, immobilizing the polynucleotide-targeting element-separation group via the incorporated ddNTP (Column 7, lines 5-32; Column 9, lines 36-53 and Claim 18, steps a-g).

Regarding Claim 40, Ju et al disclose the method wherein the oligonucleotide targeting element comprises an extendable 3' hydroxy terminus (i.e. primer, Column 5, lines 3-11).

Regarding Claim 41, Ju et al disclose the method wherein attachment of the separation group to the oligonucleotide is covalent (Column 6, lines 36-47).

Regarding Claim 42, Ju et al disclose the method wherein the first separation group is attached to the targeting element by extending the oligonucleotide with a polymerase in the presence of biotinylated nucleotide forming an extended oligonucleotide containing immobilizable nucleotide (Column 6, lines 17-47).

Regarding Claim 43, Ju et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules (i.e. mixture of differently sized primer extension products, Column 6, lines 13-47) comprising the polynucleotide having a first target sequence within 100 nucleotides of a distinguishing element (primer binding site adjacent to site of terminator incorporation, Column 5, lines 11-13), contacting the population of nucleic acid molecules with a first targeting element (i.e. primer) which specifically binds to the polynucleotide molecule, selectively and covalently attaching a separation group comprising an immobilizable nucleotide (biotinylated ddNTP) to the targeting element bound to the polynucleotide wherein the attaching only occurs when the primer is bound to the polynucleotide, immobilizing the polynucleotide-targeting element-separation group via the incorporated ddNTP (Column 7, lines 5-32; Column 9, lines 36-53 and Claim 18, steps a-g).

Regarding Claim 44, Ju et al disclose the method wherein the sequence of interest is an amplified sequence (Column 6, lines 17-31).

Regarding Claim 45, Ju et al disclose the method wherein the attachment occurs through ligation i.e. primer extension ligates nucleotides to the 3' hydroxyl (Column 6, lines 17-47). It is noted that the claim does not require a method step utilizing a specific ligase enzyme. As such, the ligation of the nucleotide onto the primer's 3' end is encompassed by the claimed ligation.

Regarding Claim 46, Ju et al disclose the method wherein covalent attachment occurs by polymerase extension (Column 6, lines 17-47).

Response to Comments

9. The claims have been amended to limit the target nucleic acids to genomic DNA or RNA. As cited in the previous Office Action, Engelhardt et al teaches a method similar to Ju wherein the targets are as newly claimed and further teaches the method is useful for detecting SNPs which clearly suggests that SNPs are important elements of genomic DNA (Column 2, lines 17-

23; Column 3, lines 22-45; and Column 12, lines 26-50). Therefore, use of the method taught by Ju to analyze genomic DNA and/or RNA would have been an obvious choice for one of ordinary skill in the art.

Applicant asserts that neither Ju or Engelhardt teach selective attachment of a separation group. The argument has been considered but is not found persuasive. As cited above, Ju selectively attaches a biotinylated nucleotide (Column 6, lines 31-45). This attachment is selective as claimed, because the attachment is template dependent i.e. an A is attached where the template has a T. The claims merely require "selective attachment". Because the attachment of Ju is template dependent, they teach the selective attachment as claimed.

Applicant asserts that no sufficient motivation to combine is present because the starting material of the '936 patent is not appropriate for the combination as suggested. The argument is noted. However, even if accurate, various starting materials are routinely used in various methods as evidenced by e.g. Engelhardt who cites the variety of targets used in assays and their preparation techniques (Column 1, lines 25-52). Therefore, adding a simple target purification would be routine as taught by Englehardt. However, the argument is not relevant to the instant claims because the claims are silent regarding content of the starting material except for the requirement of having genomic DNA or RNA.

Applicant asserts there is no reasonable expectation of success. Applicant states that additional steps of amplification and purification would be necessary to accomplish the combination as suggested by the office. Applicant further states that a declaration has been submitted to support this argument.

10. The Declaration under 37 CFR 1.132 filed 5 April 2005 is insufficient to overcome the rejection of claims 1, 3-12, 15-18, 21, 39-40, 42-49 based upon Ju et al in view of Engelhardt et al as set forth in the last Office action because:

The Declaration states that additional steps of amplification and purification would be required to successfully combine the methods of Ju and Englehardt. The Declaration further asserts:

> There is no indication in Ju or in Engelhardt that the method described in Ju could be adapted for a target nucleic acid that has not been cloned, as is required by the claims.

The Declaration is insufficient because it incorrectly asserts that the claims require target sequences that are not cloned. However, the claims are not so limited. Therefore, the arguments set forth in the Declaration are not commensurate in scope with the claims.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

11. Claims 53-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lundeberg et al (U.S. Patent No. 6,482,592, filed 15 September 1998).

Regarding Claims 53-54, Lundeberg et al disclose a method for separating a polynucleotide molecule from a population comprising providing a population of nucleic acid molecules comprising the polynucleotide having a first target sequence within 100 nucleotides of a distinguishing element (i.e. module-binding site), contacting the population of nucleic acid molecules with a first targeting element containing a separation group (module) which specifically binds to the polynucleotide molecule, selectively stabilizing the binding of the targeting element (via additional modules, Column 4, lines 9-11) and immobilizing the polynucleotide-targeting element-separation group complex and isolating the complex (Column

11, lines 7-14) wherein the polynucleotide of interest is genomic DNA (Column 4, lines 43-45) but they do not teach specific diagnostic application e.g. detection of single nucleotide polymorphism (SNP).

Engelhardt et al teach a similar method of separating genomic DNA of interest and they further teach the method is useful for detecting SNPs which clearly suggests that SNPs are important elements of genomic DNA (Column 2, lines 17-23 and Column 12, lines 26-50). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the SNP separation/detection of Engelhardt to the genomic DNA analysis of Lundeberg et al based on the known importance of SNPs for the obvious benefits of separating and detecting important genomic DNA as suggested by Engelhardt (Column 2, lines 17-23).

Response to Comments

12. Applicant reiterates the arguments regarding Lundeburg presented above. The arguments have been considered and not found persuasive as discussed above. Applicant asserts that the deficiency of Lundeburg is not cured by the teaching of Engelhardt. The argument is not persuasive for the reasons stated above regarding Lundeburg.

13. Claims 61 and 82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Montforte et al (WO 98/26095, published 18 June 1998) in view of Snitman (U.S. Patent No. 4,762,779, issued 9 August 1988).

Regarding Claims 61 and 82, Montforte et al disclose a method for separating a target molecule, the target comprising genomic or RNA (page 53, lines 12-15) and a target sequence and distinguishing element (e.g. SNP, page 54). The method comprising the steps of contacting a population of nucleic acids with a targeting element (probe) that binds adjacent to the mutation, and selectively and covalently attaching a separation group to the targeting element

(biotinylated nucleotide, page 55, lines 6-19), immobilizing the polynucleotide and targeting element via separation group (e.g. biotin-avidin, page 54, lines 24-29) and removing the immobilized complex from the population of nucleic acids i.e. partitioning (pages 54-56). Montforte et al teach the separation group comprises a modified nucleotide (page 6, lines 16-31) but they do not teach modification of a fluorescein for capture by anti-fluorescein-coated beads. However, this method of nucleotide capture was well known in the art as taught by Snitman. Snitman specifically teaches that anti-fluorescein coated bead capture of fluorescein modified nucleotides is more stable and efficient when compared to biotin capture (Column 11, lines 1-50). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the biotin capture of Montforte et al with the fluorescein/anti-fluorescein capture taught by Snitman for the expected benefits of increased stability and efficiency as taught by Snitman (Column 11, lines 1-50).

14. Claims 65-67, 69, 86-88 and 90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Montforte et al (WO 98/26095, published 18 June 1998) in view of Beattie et al (U.S. Patent No. 6,268,147, filed 2 November 1999).

Regarding Claims 65-67, 69, 86-88 and 90, Montforte et al disclose a method for separating a target molecule, the target comprising genomic or RNA (page 53, lines 12-15) and a target sequence and distinguishing element (e.g. SNP, page 54). The method comprising the steps of contacting a population of nucleic acids with a targeting element (probe) that binds adjacent to the mutation, and selectively and covalently attaching a separation group to the targeting element (biotinylated nucleotide, page 55, lines 6-19), immobilizing the polynucleotide and targeting element via separation group (e.g. biotin-avidin, page 54, lines 24-29) and removing the immobilized complex from the population of nucleic acids i.e. partitioning (pages

54-56). Montforte et al further teach the method wherein the beads are washed to remove complex (page 11, lines 28-32) but they do not teach the extension product comprises multiple separation groups. However, Beattie et al teach a similar method of genotyping wherein multiple separation groups (stacking probes coupled to distinguishable beads) are added to the target molecule (Example 18) wherein the extension product and polynucleotide is immobilized via the separation groups (Fig. 15 A & B) and wherein the combination of multiple separation groups provides for a "high degree of multiplexing" (Column 40, lines 21-28). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the separation group immobilization of Montforte et al with the multiple separation groups as taught by Beattie et al for the expected benefit of achieving a "high degree of multiplexing" as taught by Beattie et al (Column 40, lines 21-28).

15. Claims 70, 91 and 98-101 are rejected under 35 U.S.C. 103(a) as being unpatentable over Montforte et al (WO 98/26095, published 18 June 1998) in view of Jones (U.S. Patent No. 5,858,671, filed 1 November 1996).

Regarding Claims 70, 91 and 98-101, Montforte et al disclose a method for separating a target molecule, the target comprising genomic or RNA (page 53, lines 12-15) and a target sequence and distinguishing element (e.g. SNP, page 54). The method comprising the steps of contacting a population of nucleic acids with a targeting element (probe) that binds adjacent to the mutation, and selectively and covalently attaching a separation group to the targeting element (biotinylated nucleotide, page 55, lines 6-19), immobilizing the polynucleotide and targeting element via separation group (e.g. biotin-avidin, page 54, lines 24-29) and removing the immobilized complex from the population of nucleic acids i.e. partitioning (pages 54-56). Montforte teaches their method comprises multiplexing (Example 6) but they are silent regarding the format for performing the method. However, automated high-throughput and

miniaturized formats were well known in the art at the time the claimed invention was made as taught by Jones who teach the automated high thought put formats using miniaturized formats e.g. chips facilitate analyzing of multiplex reactions e.g. polymorphism identification (Column 4, lines 322-33). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the miniaturized and high throughput formats of Jones to the multiplex polymorphic analysis of Montforte et al for the expected benefit of facilitating identification of polymorphisms as taught by Jones (Column 4,lines 25-27). Jones further teaches the method comprising shaking the beads (i.e. providing relative movement) reduces steric hindrance (Column 17, lines 12-25). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the shaking of Jones to the bead assays of Montforte for the expected benefit of reducing steric hindrance during the assay as taught by Jones (Column 17, lines 12-25).

16. Claims 73-74 and 94-95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Montforte et al (WO 98/26095, published 18 June 1998) in view of Radding et al (U.S. Patent No. 4,888,274, issued 19 December 1989).

Regarding Claims 73-74 and 94-95, Montforte et al disclose a method for separating a target molecule, the target comprising genomic DNA or RNA (page 53, lines 12-15) and a target sequence and distinguishing element (e.g. SNP, page 54). The method comprising the steps of contacting a population of nucleic acids with a targeting element comprising a covalently attached separation group (biotinylated nucleotide) that binds adjacent to the mutation, and stabilizing the binding of the targeting element (i.e. the primer extension or ligation increases stability, page 59, lines 3-10), immobilizing the polynucleotide and targeting element via

separation group (e.g. biotin-avidin, page 54, lines 24-29) and removing the immobilized complex from the population of nucleic acids i.e. partitioning (pages 54-56). Montforte teaches stabilized complexes (page 59, lines 3-10) but they do not teach using a DNA binding protein e.g. RecA to obtain their desired stability. However, RecA stabilization of hybrid nucleic acids was well known in the art at the time the claimed invention was made as taught by Radding et al who teaches that RecA facilitates formation of a specific and stable duplex and provides for enrichment of target DNA (Abstract). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to add the RecA of Radding to the duplex formation of Montforte for the expected benefit of facilitating specific and stable duplex formation and target DNA enrichment as taught by Radding (Abstract).

Conclusion

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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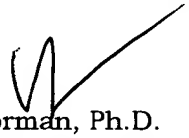

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Art Unit: 1634
June 9, 2005